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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,133	05/09/2006	Michael Didriksen	447-US-PCT	5885

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LUNDBECK RESEARCH USA, INC.
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EXAMINER	
RAMACHANDRAN, UMAMAHESWARI	
ART UNIT	**PAPER NUMBER**
1617	
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07/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/568,133	DIDRIKSEN ET AL.	
	Examiner	Art Unit	
	Umamaheswari Ramachandran	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-17,19 and 20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-17, 19, 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner notes the receipt of the amendments and remarks received in the office on 6/1/2007. Applicants elect Group I and depression as the species from claim 1; citalopram as the species from claim 6; and N-{3-[5-Chloro-I-(4-chloro-phenyl)-indan-I-yl]-propyl}-N-methyl-alanine from claim 7. Claims 19 and 20 have been added new and claims 2 and 18 are canceled. Applicants' arguments regarding the restriction requirement has been considered and found persuasive. The restriction requirement is withdrawn and the species election is maintained. Accordingly, claims 1, 3-17, 19, 20 with the species elected will be examined. The restriction requirement is made final. Claims 1, 3-17, 19, 20 are currently pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for serotonin analysis and measurement of serotonin levels with citalopram and glycine transport inhibitor NFPS (specification, page 25-26) does not reasonably provide enablement for all disorders as listed in claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the Invention:

The rejected claims are drawn to a method of treating a disorder selected from depression, anxiety disorders, eating disorders, phobia etc as listed in claim 1 comprising administering to the person a serotonin reuptake inhibitor and a GlyT-1 inhibitor compound .

(2) Breadth of the claims:

Claims 1, 3-4 are broad and is drawn to a method of treating a disorder selected from depression, anxiety disorders, eating disorders, phobia etc as listed in claim 1 comprising administering to the person a serotonin reuptake inhibitor and a GlyT-1 inhibitor compound. The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claim.

(3) Guidance of the Specification:

The guidance given by the specification is for a method of for serotonin analysis and measurement of serotonin levels with citalopram and glycine transport inhibitor NFPS (specification, page 25-26).

(4) Working Examples:

The example in the specification provides methods for serotonin analysis and measurement of serotonin levels in hippocampus.

(5) The relative skill of those in the art:

The relative skill of those in the medical treatment art is high, requiring advanced education and training.

(6) The predictability of art:

Claims 1, 3-4 is drawn to a method of treating a disorder selected from depression, anxiety disorders, eating disorders, phobia etc as listed in claim 1 comprising administering to the person a serotonin reuptake inhibitor and a GlyT-1 inhibitor compound. Claims 1, 3-5 are so broad and there is a high degree of unpredictability involved. Despite the advanced training in the medical treatment arts, the arts are highly unpredictable.

(7) The Quantity of Experimentation Necessary:

In order to practice the above claimed invention, one of skill in the art would have to first envision formulation, dosage, duration, route and, in the case of human treatment, an appropriate animal model system for the treatment of every single disorder listed in claim1 with every single SSRI and GlyT-1 inhibitor combination. If unsuccessful, one of skill in the art would have to envision a modification in the

formulation, dosage, duration, route of administration etc. and appropriate animal model system, or envision an entirely new combination of the above and test the system again. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention of treating the disorders listed in claim1. Applicant fails to provide information sufficient to practice the claimed invention, absent undue experimentation. Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement in a method of treating a disorder listed in claim 1 with all serotonin reuptake inhibitors and GlyT-1 inhibitors. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set

forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the Invention:

The rejected claims are drawn to a method of treating a disorder selected from depression, anxiety disorders, eating disorders, phobia etc as listed in claim 1 comprising administering to the person a serotonin reuptake inhibitor and a GlyT-1 inhibitor compound .

(2) Breadth of the claims:

Claims 1, 3-5 are broad and is drawn to a method of treating a disorder selected from depression, anxiety disorders, eating disorders, phobia etc as listed in claim 1 comprising administering to the person a serotonin reuptake inhibitor and a GlyT-1 inhibitor compound. The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claim.

(3) Guidance of the Specification:

The guidance given by the specification is for a method of for serotonin analysis and measurement of serotonin levels with citalopram and glycine transport inhibitor NFPS (specification, page 25-26).

(4) Working Examples:

The example in the specification provides methods for serotonin analysis and measurement of serotonin levels in hippocampus with citalopram and glycine transport inhibitor NFPS. The specification does not provide examples with any other SSRI and GlyT-1 inhibitor combination in a method of treating a disorder or in serotonin analysis or measurement of serotonin.

(5) The relative skill of those in the art:

The relative skill of those in the medical treatment art is high, requiring advanced education and training.

(6) The predictability of art:

Claims 1, 3-5 is drawn to a method of treating a disorder selected from depression, anxiety disorders, eating disorders, phobia etc as listed in claim 1 comprising administering to the person a serotonin reuptake inhibitor and a GlyT-1 inhibitor compound. The method of treatment comprises the administration of an SSRI and a GlyT-1 inhibitor in combination and there is a high degree of unpredictability involved. Despite the advanced training in the medical treatment arts, the arts are highly unpredictable.

(7) The Quantity of Experimentation Necessary:

In order to practice the above claimed invention, one of skill in the art would have to first envision formulation, dosage, duration, route and, in the case of human treatment, an appropriate animal model system for the treatment of every single SSRI and GlyT-1 inhibitor combination for every single disorder listed in claim1. If

unsuccessful, one of skill in the art would have to envision a modification in the formulation, dosage, duration, route of administration etc. and appropriate animal model system, or envision an entirely new combination of the above and test the system again. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention of treating the disorders listed in claim 1 administering SSRI and GlyT-1 combination therapy. Applicant fails to provide information sufficient to practice the claimed invention, absent undue experimentation. Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-14, 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coppen (U.S. 6,191,133) in view of Lowe (U.S. 6,506,780) and further in view Moltzen et al. (U.S. 2003/0181,445, effective filing date, July 19 2001) and further in view of Mork et al. (U.S. 2005/0288355, effective filing date, Jun 19 2003).

Coppen teaches specific formulation for the treatment of depression comprising serotonin reuptake inhibitors (SSRI) such as citalopram (col.8, example 5). The

reference teaches a method of treating depression in a patient comprising administering to the patient a therapeutically effective amount of an anti-depressive compound selected from the class of compounds comprising serotonin reuptake inhibitors and teaches citalopram as one of the anti-depressants (col. 10, claims 6-10). The reference teaches SSRI inhibitors and the second agent folate in the same dosage unit forms as tablets and further teaches that SSRI can be administered simultaneously with another agent such as folate (col. 10, claim 10).

The reference does not teach a GlyT-1 inhibitor in the composition comprising serotonin reuptake inhibitor for the treatment of depression.

Lowe et al. teach that compounds that exhibit activity as inhibitors of glycine type I transporter are useful in the treatment of depression (col. 1, lines 10-14). The reference further teaches a pharmaceutical composition comprising the GlyT-1 inhibitor and a method of treating a disorder or condition such as psychosis, psychotic disorders, and depression etc. administering GlyT-1 inhibitor compounds (col. 33-36, claims 1-16).

The reference does not teach the elected species N-{3-[5-Chloro-l-(4-chloro-phenyl)-indan-l-yl]-propyl}-N-methyl-alanine as the GlyT-1 inhibitor in the composition in a method of treating depression.

Moltzen et al. teaches a pharmaceutical composition comprising GlyT-1 inhibitor such as N-{3-[5-Chloro-l-(4-chloro-phenyl)-indan-l-yl]-propyl}-N-methyl-alanine (elected species) in a therapeutically effective amount with one or more of pharmaceutically acceptable carrier/diluents (para 0084, col. 11, claim 9) with a inhibition of glycine below 20000 nM (IC 50 in the glycine uptake test is 470, p10, Table). The reference further

teaches a method of treatment of psychoses, comprising administering to a patient the above said pharmaceutical composition (col. 11, claims 10, 11).

The references do not teach a method for augmenting and/or providing faster onset of the therapeutic effect of a serotonin reuptake inhibitor in a person comprising administering a serotonin reuptake inhibitor and a GlyT-1 inhibitor compound.

Mork et al. teach a method of augmenting and/or providing faster onset of the therapeutic effect of a serotonin reuptake inhibitor comprising administering a second agent such as GABA receptor antagonist in a method of treatment of disorders such as depression (p 9, col. 2, claims 1-4). The reference also teaches in the background there is the delay in therapeutic effect of SSRIs (para 004) and augmentation therapy is done in order to cope with non-response to SSRI's (para 005, 003).

It would have been obvious to one of ordinary skill in the art at the time of the invention to administer serotonin reuptake inhibitors (SSRI) such as citalopram (elected species) along with a GlyT-1 inhibitor in a method of treatment of depression. The motivation to do so is provided by Coppen, Lowe, Moltzen and Mork et al. The references in combination teach both SSRI and GlyT-1 inhibitor in a method of treatment of depression. Coppen specifically teaches the benefits of the elected species citalopram in the treatment of depression. Moltzen teach GlyT-1 inhibitor (elected species) in a method of treatment of psychoses and Lowe exemplify the use of GlyT-1 inhibitors in a method of treatment of depression. Finally Mork teaches the use of citalopram in depression disorder treatment and further teaches the beneficial effects of combination therapy to augment or to provide a faster onset of the therapeutic effect of

an SSRI by adding a second agent. The Moltzen reference does not specifically teach the elected species of GlyT-1 inhibitor (N-{3-[5-Chloro-l-(4-chloro-phenyl)-indan-l-yl]-propyl}-N-methyl-alanine) in a method of treatment of depression but teaches the elected compound in a method of psychosis. Stedman medical dictionary defines psychosis as 'A severe mental disorder, with or without organic damage, characterized by derangement of personality and loss of contact with reality and causing deterioration of normal social functioning'. It is known that people who have psychosis often are depressed and psychotic depression is a type of depression disorder. One of ordinary skill in the art would have been motivated to use GlyT-1 inhibitor (N-{3-[5-Chloro-l-(4-chloro-phenyl)-indan-l-yl]-propyl}-N-methyl-alanine, the elected species) in a method of treatment of depression because Moltzen teaches the compound as GlyT-1 inhibitor and in a method of treatment of psychoses and Lowe teaches the use of GlyT-1 inhibitors in a method of treatment of depression. Hence one of ordinary skill in the art would have been motivated to combine citalopram and a GlyT-1 inhibitor in a composition to treat a disorder such as depression because the teachings show the therapeutic benefits and safety of such drugs in the treatment of depression. The examiner respectfully points out the following from MPEP 2144.06: "It is **prima facie obvious** to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose....[T]he idea of combining them flows logically from their, having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069,-1072 (CCPA 1980).

One of ordinary skill in the art at the time of the invention would have been motivated to have added another agent such as GlyT-1 inhibitor to SSRI to provide augmentation and or to provide faster onset of therapeutic effect of SSRI because it can offset the delay in the therapeutic effects of SSRI's or to cope up with non-response to SSRI's as taught by Mork et al.

Claims 13-16, 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coppen (U.S. 6,191,133) in view of Lowe (U.S. 6,506,780) and further in view Moltzen et al. (U.S. 2003/0181,445, effective filing date, July 19 2001) and further in view of Mork et al. (U.S. 2005/0288355) as applied to claims 1, 3-12, 19 above and further in view of Carlson et al. (U.S. 6,649,614).

Coppen, Lowe, Moltzen and Mork et al.'s teachings discussed as above.

The references do not teach the pharmaceutical composition adapted for sequential administration or the active ingredients in discrete dosage forms.

Carlson et al. teach the treatment of depression comprising administering a combination of an antidepressant such as SSRI and an NK-1 receptor antagonist (see abstract, col.2, line 49). The reference teaches citalopram as one of the antidepressants in the treatment (col.6, line 26). The reference teaches the composition in unit dosage forms such as tablets, pills etc (col. 34, lines 43-45) and further teaches that in combination therapy the compounds may be in the same pharmaceutically acceptable carrier for simultaneous administration or in separate dosage forms for sequential administration (col. 3, lines 61-67).

It would have been obvious to one of ordinary skill in the art at the time of the invention to have provided a pharmaceutical composition comprising SSRI and a GlyT-1 inhibitor adapted for sequential administration or the active ingredients in discrete dosage forms for the treatment of depression. One of ordinary skill in the art would have been motivated to do so is by the teachings of Carlson. The reference teaches a method of treatment of depression comprising a composition in unit dosage forms, separate dosage forms and further teaches the mode of administration (sequential, simultaneous). Hence one of ordinary skill in the art would have expected similar success and it is also part of routine experimentation to try various modes of administration and dosage forms. The examiner respectfully points out the following from MPEP 2144.05: "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." I*n re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); *In re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969); Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 USPQ2d 1056 (Fed.Cir. 1990); and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Coppen (U.S. 6,191,133) in view of Lowe (U.S. 6,506,780) and further in view Moltzen et al.

(U.S. 2003/0181,445, effective filing date, July 19 2001) and further in view of Mork et al. (U.S. 2005/0288355) as applied to claims 1, 3-12, 19 above and further in view of Gupta et al. (US 2005/0014743), Remington's: the Science and Practice of Pharmacy, Nineteenth edition, vol. 1, p 806.

Coppen, Lowe, Moltzen and Mork et al.'s teachings discussed as above.

The references do not teach a kit comprising a serotonin reuptake inhibitor, GlyT-1 inhibitor and optionally a pharmaceutical carrier.

Gupta et al. teach a method of treatment of depression using SSRI such as citalopram in a combination therapy and further teaches a kit comprising SSRI and other active agents (See Abstract, p 11, para 0242) for the treatment.

It would have been obvious to one of ordinary skill in the art at the time of the invention to provide a kit comprising SSRI and GlyT-1 inhibitor. One of ordinary skill in the art would have been motivated to provide a kit because Gupta et al. teaches one comprising SSRI and other active agents and providing kits helps patients to take the drugs with ease as per the instructions in the kit.

Remington's: the Science and Practice of Pharmacy, Nineteenth edition, vol. 1, p 806 teaches the at the inclusion of package and insert including the "indications and use" of the pharmaceutical composition is mandated by 21 CFR 201.57.

One of ordinary skill in the art would have been motivated to include the packaging and the insert because they have been mandated by the law as taught by Remington's.

The examiner respectfully points out the following from MPEP 2106.01: "Where the printed matter is not functionally related to the substrate, the printed matter will not distinguish the invention from the prior art in terms of patentability." In re Ngai (70 USPQ2d 1862).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Umamaheswari Ramachandran whose telephone number is 571-272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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SREENI PADMANABHAN
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